UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,473	11/13/2007	Xian-Ming Zeng	TEVE-124US	9501

23122 7590 05/07/2012
RATNERPRESTIA
P.O. BOX 980
VALLEY FORGE, PA 19482-0980

EXAMINER	
SINGH, RANDEEP	
ART UNIT	PAPER NUMBER
1615	
MAIL DATE	DELIVERY MODE
05/07/2012	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,473	ZENG ET AL.	
	Examiner	Art Unit	
	RANDEEP SINGH	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2012*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-15* is/are pending in the application.

5a) Of the above claim(s) *11 and 12* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-10 and 13-15* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/04/2012*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/04/2012 has been entered.

Status of Claims

Claims 1-10 and 13-15 are pending and have been examined in this action. Claim 1 has been amended. Claims 13-15 have been newly added. Claims 1-10 and 13-15 are rejected.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 04/04/2012 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner. Please see attached initialed PTO-1449 form.

Previous Rejections

Applicants' arguments filed 04/04/2012 have been fully considered and were found persuasive.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections are newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 6, 7, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Ikegami et al. (cited in Applicants' IDS dated 04/04/2012).

Regarding claim 1, Ikegami et al. disclose the preparation of agglomerates of KSR-592, which is a dry powder inhalation steroid (i.e., a pharmaceutically active ingredient) (see page 324, paragraph 2.1). The agglomerates were produced under three different sets of conditions and the median diameter of the agglomerates obtained under the different conditions was about 200-250 μm (see page 326, paragraph 3.1 and Figure 2). Such agglomerates are clearly capable of passing through a sieve having a mesh of 50-3000 μm. Ikegami et al. also disclose combining the agglomerates of KSR-

592 with lactose (carrier) and mixing the resultant mixture in a blender equipped with two blades (see page 325, paragraph 2.3). Upon mixing, the agglomerates disintegrated into the primary particles and for one set of agglomerates (prepared at 5℃/1000 r.p.m) the median diameter of the agglomerates decreased from 250 to 2.4 μm (see pages 327 and 328, paragraph 3.2 and pages 331 and 332, paragraph 4). Thus, the mixing step in the process of Ikegami et al. breaks up the KSR-592 agglomerate into primary particles dispersed in the carrier such that 90% or more of the active exists as primary particles having a particle size of 50 μm or less. As such, this disclosure of Ikegami et al. anticipates claim 1.

Regarding the specific limitations of claim 2, Ikegami et al. disclose a process comprising all the steps of claim 1. Therefore, it is inevitable that the process of Ikegami et al. would produce a medicament in which the active is dispersed homogeneously in the carrier such that the drug recovery of each of a plurality of samples taken from the medicament has a relative standard deviation from the mean of less than or equal to 5%. As such, the disclosure of Ikegami et al. anticipates claim 2.

Regarding the specific limitations of claim 4, Ikegami et al. disclose agglomerates with a median diameter of about 200-250 μm (see page 326, paragraph 3.1 and Figure 2), which would be capable of passing through the mesh specified in claim 4. As such, the disclosure of Ikegami et al. anticipates claim 4.

Regarding the specific limitations of claims 6 and 7, Ikegami et al. disclose the preparation of agglomerates of KSR-592, which is a dry powder inhalation steroid (see page 324, paragraph 2.1). This disclosure of Ikegami et al. anticipates claims 6 and 7.

Regarding the specific limitations of claim 9, Ikegami et al. disclose combining the agglomerates of KSR-592 with lactose as a carrier. This disclosure of Ikegami et al. anticipates claim 9.

Regarding the specific limitations of claims 3 and 5, Ikegami et al. do not explicitly recite passing a pharmaceutically active ingredient though a sieve having a mess of 50-3000 μm prior to combining the pharmaceutically active ingredient with a carrier.

Regarding the specific limitations of claim 8, Ikegami et al. do not explicitly recite budesonide, formoterol, or etiprednol as inhalable medicaments.

Regarding the specific limitations of claim 10, Ikegami et al. do not explicitly recite alpha-lactose monohydrate as a pharmaceutically acceptable carrier.

Regarding the specific limitations of claims 13-15, Ikegami et al. do not explicitly recite multidose dry powder inhalers, or reservoirs that are capsules which, when filled, contain a unit dose of active ingredient.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-10 and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ikegami et al. (cited above) in view of De Villiers et al. (cited in Applicants' IDS dated 04/04/2012), further in view of Bell (cited in Applicants' IDS dated 04/04/2012), Trofast et al. (cited in Applicants' IDS dated 04/04/2012), Zeng (WO2004017918, cited in Applicants' IDS dated 04/04/2012), and Bystrom (cited in previous action).

De Villiers et al. investigate the rate of furosemide agglomerate deaggregation during interactive mixing with a carrier in the preparation of a medicament (see page 1391, first and second paragraphs and the paragraph bridging pages 1391 and 1392). De Villiers et al. disclose a process in which furosemide (active) agglomerates from the sieve fraction 500-700 µm were mixed with either sodium chloride or Avicel pH102 particles (carriers) in a Turbula mixer (see page 1392, paragraphs entitled "Mixing Components" and "Mixing"). The furosemide agglomerates are clearly capable of passing through a sieve having a mesh of 50-3000 µm. De Villiers et al. teach that the furosemide agglomerates were deaggregated during mixing, as evidenced by the

increase in dissolution rate with increased mixing time, and that single particles and small aggregates are formed (see page 1396, final two paragraphs).

De Villiers et al. do not explicitly state that the agglomerate is broken down such that 90% or more of the active exists as primary particles having a particle size of 50 μm or less. It would, however, have been obvious to one of ordinary level of skill in the art at the time of the invention to mix the agglomerates of active with the carrier so as to provide such primary particles because it was well known at the time of the invention that such particle sizes are required for efficient administration to the lungs. For example, Ikegami et al. (cited above) discloses primary particles having a median diameter of 2.4 μm and state in the introduction section that for dry powder inhalations to be deposited on the target site in the respiratory tract it is required that the particle size of the drug formulation be 0.5 to 0.7 μm (see page 323, paragraph 1 and pages 327 and 328, paragraph 3.2). Furthermore, Bell teaches that for administration by inhalation greater than 95% by weight of the particles must have a diameter of less than 10 microns, for example from 0.01 to 10 and preferably from 1 to 4 microns (see column 2, lines 11-17). Also, Trofast et al., which teach powdered medicaments for inhalation therapy, teach that the diameter of particles to be inhaled must be less than 10 μm or the particles will not adequately penetrate the bronchial area of the lungs (see column 1, lines 11-14). Thus, claim 1 would have obvious at the time of the invention in view of the combined teachings of Ikegami et al., De Villiers et al., Bell, and Trofast et al.

Regarding claims 3 and 5, it was well known at the time of the invention to form an agglomerate of a specific size by passing an active through a sieve having a mesh of a specified size. For example, De Villiers et al. and Bell teach a process in which agglomerates are formed by sieving and which use meshes of the sizes specified in claims 3 and 5. Additionally, Trofast et al. disclose a method of forming agglomerations that includes the step of forcing a powder through a sieve to form agglomerates and teach that the size of the mesh used determines the size of agglomerates formed (see column 1, lines 61-64; column 2, lines 15-17; column 3, lines 3-5 and 21-26; and column 5, lines 19-21). Thus, it would have been obvious to one of ordinary level of skill in the art at the time of the invention to pass a pharmaceutically active ingredient through a sieve to form an agglomerate prior to combining it with a carrier, based on the combined teachings of De Villiers et al., Bell, and Trofast et al.

Regarding the specific limitations of claim 8, Zeng discloses methods for preparing dry powder inhalation compositions comprising a carrier and a medicament. In Example 1, Zeng teaches combining budesonide (active agent) and lactose carrier in a mixing vessel for the formation of agglomerates for dry powder inhalable medicaments. Based on the teachings of Zeng, it would have been obvious to one of ordinary level of skill in the art at the time of the invention to include budesonide as an active agent in the processes disclosed by the combined teachings of Ikegami et al., De Villiers et al., Bell, and Trofast et al. for the formation of a dry powder medicament.

Regarding the specific limitations of claim 10, Bystrom discloses a homogenous molecular mixture of a biologically active component and a lipid (carrier) (see column 2, lines 35-38). Bystrom discloses lactose monohydrate as a preferred carrier in inhalable medicaments (see column 4, lines 40-41). Based on the teachings of Bystrom, it would have been obvious to one of ordinary level of skill in the art at the time of the invention to include lactose monohydrate as a carrier in the processes disclosed by the combined teachings of Ikegami et al., De Villiers et al., Bell, and Trofast et al. for the formation of a dry powder medicament.

Regarding the specific limitations of claim 13, Zeng teaches filling a dry powder composition into the reservoir of a multidose dry powder inhaler (see paragraph [0033]) for administration to a subject. Regarding the specific limitations of claim 14, Zeng teaches filling a dry powder composition into a reservoir defined by a capsule. Regarding the specific limitations of claim 15, Zeng teaches a capsule, which, when filled, contains a unit dose of active ingredient. Based on the teachings of Zeng, it would have been obvious to one of ordinary level of skill in the art to fill the powder medicaments for inhalation disclosed by the combined teachings of Ikegami et al., De Villiers et al., Bell, and Trofast et al. into the reservoir of a multidose dry powder inhaler or a reservoir in the form of a capsule such that the capsule contains a unit dose of active ingredient, to facilitate the efficient administration of the medicaments to a subject.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RANDEEP SINGH whose telephone number is (571)270-3881. The examiner can normally be reached on Monday-Friday 10:00-6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571)272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Randeep Singh/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615